

TMH/DAG:lam 11/03/03  
PATENTAttorney Reference Number 4239-61302  
Application Number 10/017,372**REMARKS**

Claims 1-11, 18, 19, 22, 28-37, 49-52, 57 and 58 were pending in this application. Claims 10, 22, 30, 49-52, and 57 are cancelled herein. Applicants expressly reserve the right to pursue protection of any or all of the subject matter of the cancelled claims in a subsequent application. Claims 1, 2, 4, 6, 9, 11, 18, 31-35, and 58 have been amended and new claims 59-61 have been added. Six paragraphs of the specification have been amended. Support for the amendments is discussed below as needed. No new matter is introduced by these amendments.

After entry of this amendment **claims 1-9, 11, 18, 19, 28, 29, 31-37, and 58-61 are pending in this application.** Consideration of the pending claims is requested.

**Telephone Interview:**

Applicants thank Examiners Nichols and Kemmerer for the courtesy of a telephone interview with their representatives, Tanya Harding and Debra Gordon, on October 27, 2003, and for providing the Interview Summary, dated October 27, 2003. During the telephone conference, the Proposed Examiner's Amendment, dated October 20, 2003 ("Examiner's Amendment"), was discussed. The Examiner's Amendment provided a proposed set of allowable claims. To facilitate the telephone discussion, Applicants' representatives delivered proposed revisions of the Examiner's Amendment to Examiner Nichols by facsimile prior to the interview.

Applicants' representatives explained that claims 1, 31, and 33 as proposed in the Examiner's Amendment required slight revision in order to properly represent the claimed fusion proteins. In particular, Applicants proposed that (i) claim 1 should recite the amino acid residues of SEQ ID NO: 37 that correspond to the mature TGF- $\beta$ 1, and (ii) the nucleic acid sequences recited in claims 31 and 33 should not be changed from that submitted in the Amendment and Response to Non-final Office Action, filed September 17, 2003. The Examiners agreed with both proposals and stated that claims 1, 31, and 33 would be allowable as discussed in the interview and as shown in the marked-up Examiner's Amendment; provided that the Applicants provide support for the amino acid residues of the mature TGF- $\beta$ 1 recited in proposed claim 1.

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To this end, Examiner Kemmerer suggested amending Table 2 (at page 70 of the Specification) to include amino acid residues corresponding to the nucleic acid residues already shown in the table. Examiner Kemmerer stated that her suggested amendment would not introduce new matter.

Applicants further thank Examiner Nichols for a follow up telephone call to Debra Gordon on October 28, 2003. In that call, Examiner Nichols clarified that it was acceptable to delete amino acid sequences known in the prior art, such as, the endoplasmic reticulum signal (KDEL) and the Tat<sub>49-57</sub> HIV fragment (RKKRRQRRR), from the specification in lieu of adding such sequences to the Sequence Listing.

Amendments to the Specification

One paragraph on each of pages 3 and 15 and two paragraphs on page 5 of the Specification have been amended to comply with the sequence rules (37 C.F.R. §§ 1.821-1.825). Particular residues specified in these amendments may be found by reference at least to the original Sequence Listing.

One paragraph on page 63 has been amended only to correct clerical errors.

Table 2 on page 70 of the Specification has been amended to show amino acid sequences corresponding to the previously (and still) shown nucleic acid sequences. In the October 27, 2003 telephone interview, Examiner Kemmerer stated that no new matter is introduced by such an amendment.

We also corrected a few minor clerical errors found in Table 2 on page 70 of the Specification, as follows:

Row	Column	Correction	Support
1	5	This column header has been clarified to read: "AA 1-5 of <u>mature</u> TGF- $\beta$ "	At least supported by the column header and respective nucleotide positions shown in column 7.

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Row	Column	Correction	Support
2	7	The starting nucleotide position of the mature fusion protein has been corrected from "182" to "1182."	At least supported by the starting nucleotide shown in the row 2, column 5.
6	6	The last nucleic acid residue of the tag has been corrected from "945" to "933."	At least supported by the original sequence listing, wherein it is easily seen that the FLAG tag ends at nucleotide position 933.
10	1	The fusion protein name has been corrected from ...FLAG... to ...HA...	At least supported by the original specification at page 9, lines 11-12, and by the original sequence listing, wherein it is easily seen that the SEQ ID NOs: 36 and 37 contain an HA tag.
11	1	The fusion protein name has been corrected from ...FLAG... to ...HA...	At least supported by the original specification at page 9, lines 15-16, and by the original sequence listing, wherein it is easily seen that the SEQ ID NOs: 38 and 39 contain an HA tag.

#### Amendments to the Claims

Claim 1 has been amended to recite, in relevant part, "a mature TGF- $\beta$ 1 comprising residues 279-283 and 296-408 of SEQ ID NO: 37, or an amino acid sequence that has at least 95% sequence identity with residues 279-283 and 296-408 of SEQ ID NO: 37 and which retains TGF- $\beta$ 1 activity . . . ." The mature TGF- $\beta$ 1 recited in the above claim 1 excerpt does not contain a tag; instead, a peptide tag is a separate element of the claimed functional TGF- $\beta$ 1 fusion protein. Thus, the residues of SEQ ID NO: 37 that are recited in amended claim 1 describe only the portion of SEQ ID NO: 37 that corresponds to the mature TGF- $\beta$ 1 protein. This amendment is supported, at least, by row 10 of Table 2 wherein the sequences shown in SEQ ID NOs: 36 and 37 are parsed. The mature *fusion* protein (*i.e.*, mature TGF- $\beta$ 1 plus tag) is shown to be residues 279-408 and the tag of the same fusion protein is shown to be residues 284-295. Thus, one of ordinary skill in the art could very easily determine that residues 279-283 and 296-408 correspond to the mature TGF- $\beta$ 1 portion of the fusion protein shown in SEQ ID NO: 37.

New claims 59-61 are supported, at least, by Table 2 and the original Sequence Listing.

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All of the other claim amendments were proposed in the Examiner's Amendment; thus, Applicants believe such claim amendments to be acceptable and to introduce no new matter.

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### CONCLUSION

It is respectfully submitted that the present claims are in a condition for allowance. If it may further issuance of these claims, the Examiner is invited to call the undersigned at the telephone number listed below.

Respectfully submitted,

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